SHORT REPORT

Is the frequency of multiple sclerosis increasing in Mexico?

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Abstract
Multiple sclerosis has steadily increased in Mexican mestizos from an apparently rare disorder in the 1970s to the second most frequent cause of admission to a neurology ward in the 1990s. Most patients belonged to high socioeconomic and educational groups. Familial incidence was low. Age at onset was younger than in other series and long term disability was milder than in patients from countries in which the disease is apparently more prevalent.

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Mexico has traditionally been considered an area with a very low incidence of multiple sclerosis.[1][2] As with other countries, however, previously regarded as having a low incidence, there is a growing concern about an increase in the number of cases seen in recent years.[3] In countries where multiple sclerosis is more common the racial, geographical, nutritional, and sociocultural features, are different from Mexico. Mexican mestizos belong to a complex racial mixture; Mongoloid, in whom multiple sclerosis is rare and Caucasian, in whom it is more common.[4][5]

The question of whether multiple sclerosis is really increasing in Mexico is difficult to answer due to the lack of comparative epidemiological studies. The only study—on government employees in 1972—reported a prevalence of 1·6 per 100 000, one of the lowest at that time.[1] At the National Institute of Neurology and Neurosurgery of Mexico (NINNM) there has been a progressive increase in the number of cases of multiple sclerosis seen during the past 20 years. We first reported such an increase in 1981[3] and this trend has continued.

Patients and methods

From January 1973 until December 1992, the diagnosis of multiple sclerosis was contemplated in 358 Mexican mestizos attending the NINNM, of whom 272 fulfilled the diagnostic criteria of clinically definite multiple sclerosis.[6] To study the long term evolution of the disease, in 1993 all patients that had ceased to attend the hospital were recalled by mail, telephone, or domiciliary search; 107 patients were lost at follow up, most because they had changed address (84 cases) or lived in remote areas of the country. Although 165 patients could be followed up to 1993 for a mean of 57 (SD 7) months (range 12 to 138 months) this figure includes 20 patients who died as a consequence of multiple sclerosis. Thus in a cross sectional retrospective analysis we studied several multiple sclerosis variables in a group of 272 patients and, in a longitudinal analysis, other variables of evolution were studied in a subgroup of 165 patients. To contrast some demographic variables in patients with multiple sclerosis with a representative population, the following controls were studied: socioeconomic status was determined in 452 neurological patients selected at random from all medical records obtained during 1982–92 excluding those patients with multiple sclerosis. Educational status was determined in 650 consecutive neurological patients with diagnoses other than multiple sclerosis. We also compared clinical and laboratory findings of multiple sclerosis in Mexicans with similar studies reported from countries in which multiple sclerosis is more prevalent.

Results

As several variables were scrutinised, data obtained that showed no differences from other reports or were not apparently related to multiple sclerosis are not described unless they hold some interest. Electrophysiological studies and laboratory data on CSF were similar to other reports; MRI findings have been reported elsewhere.[7] All patients were Mexican mestizos (subjects whose parents were born in Mexico; they have a highly variable mixture of European (mostly Spanish) and Indian ancestors). Male-female ratio was 0·6:1. Mean age at the time of onset of multiple sclerosis was 27 (SD 3) years. In both instances, the educational status and socioeconomical status of patients with multiple sclerosis were higher than those of con-

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Discontinuous line represents the time of onset of multiple sclerosis (MS). Continuous line represents the time in which the patients were studied at the NINNM. Multiple sclerosis started after 1987 in 96 (62%) of those patients studied during the past five years. Numbers in parentheses represent the total number of new neurological cases studied in that period.
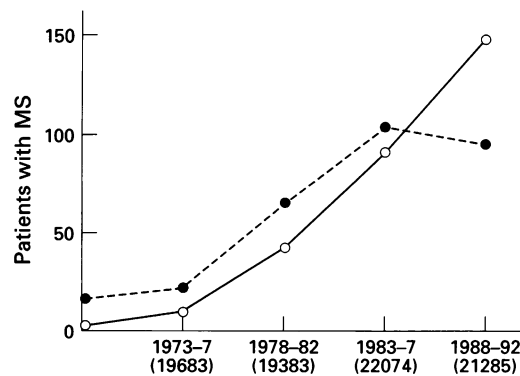
Socioeconomic and educational status in patients and controls*

	Patients with multiple sclerosis (%)	Controls (%)
Socioeconomic status:	(n = 272)	(n = 452)
High	17	7**
Middle	76	26**
Low	7	67**
Educational status	(n = 272)	(n = 650)
Professional	29	13**
First degree/technical	35	24**
High school	18	19
Basic primary school	15	37**
Illiterate	3	7**

**P < 0·001.

trols (P < 0·001; table). Nine patients (3·3%) had first and second degree relatives (four brothers and five cousins) with multiple sclerosis; parent-sibling familial multiple sclerosis was not found. The figure shows the time at which the disease started and the time of first consultation at the hospital; in 33 patients (12%) the disease started before 1978, in 239 patients (88%) the disease started during the past 15 years; the delay between disease onset and time of first consultation at the NINNM varied from three months to 15 years, with a mean of 3·8 (SD 1) years. The first sign of multiple sclerosis was optic neuritis in 28% of patients; the most common sign at long term evolution was pyramidal in 65% of patients. In the subgroup of 165 patients with long term follow up, life table analysis of disability by the expanded disability status scale (EDSS)[8] showed that 14, 24, and 27% of the population reached stage 6 (ambulatory but requiring walking aids) at 5, 10, and 15 years from onset of multiple sclerosis respectively. Key levels of the EDSS at final consultation showed minimal disability (< 4 points) in 52%; moderate disability (4 to 6 points) in 30%; and severe disability including death secondary to multiple sclerosis (7 to 10 points) in 18% of cases. Overall mortality attributed to complications of multiple sclerosis was 12% after a mean of 10·2 (SD 2) years from onset.

Discussion

Mean age of onset of multiple sclerosis, 27 years, was younger than the mean age (over 30 years) reported in most studies from other countries.[9-12] Similarly to Asian patients, optic neuritis in Mexicans was more common than

in western patients,[12] but by contrast with Asian patients, the acute syndromes of massive monophasic demyelination were rare in Mexicans. Mortality after 10 years of follow up was 12%, similar to the 13% reported in Scotland.[13] Although results from the longitudinal survey must be taken cautiously in view of the fact that only 165 of 272 patients (61%) could be followed up the long term analysis of disability showed that Mexican patients have a better outcome than that reported in other studies.[9 14] This could be related to the high frequency of optic neuritis as the initial symptom of multiple sclerosis and younger age at onset seen in our patients; both features have been associated with a favourable evolution of multiple sclerosis[9 14-16]; in 32% of our patients, multiple sclerosis started before the age of 20, whereas in other studies the proportion is between 12 and 16%.[9 12] Immunogenetic studies previously reported by us[4] have shown a significantly high frequency of the DRw6 antigen in Mexican patients, similar to results for Japanese patients with multiple sclerosis[17]; also, the HLA combination A3, B7, and DR2 was high and similar to that found in western cases[18] thus showing the heterogeneity of multiple sclerosis in Mexican mestizos.

Findings from this study suggest a real increase in the number of patients with multiple sclerosis in Mexico. For the past 20 years the mean number of new neurological patients seen every year at the NINNM has not increased significantly—around 4000 new neurological cases studied each year— whereas the yearly number of cases has steadily increased (figure). By contrast, yearly frequencies of other chronic and severe neurological disorders such as amyotrophic lateral sclerosis and myasthenia gravis have remained fairly stable for the same period, between nine and 14 new cases of amyotrophic lateral sclerosis and between 15 and 20 new cases of myasthenia gravis each year during the past 15 years. Medical attention at the NINNM is sought by people from all social classes, but the underprivileged constitute its main customer as a reflection of the social distribution in the country. It is interesting that in the case of multiple sclerosis, the relation is an inverse one; the highest proportion of patients belong to the higher socioeconomic and educational ranks (table), giving further support to a similar finding made in endemic areas of wealthy countries, where multiple sclerosis is also more prevalent among the more affluent groups.[19] This feature suggests the appearance of multiple sclerosis as part of the range of diseases associated with economic and educational affluence in the epidemiological transition from underdevelopment to development.

A clear transition of multiple sclerosis has been observed at the NINNM in the past 20 years, from a rare disease in the 1970s to the second most frequent cause of admission to the neurology ward in the 1990s. From 1964 to 1976 only nine cases of multiple sclerosis were studied; from 1977 to 1992, 263 cases

were studied, a 29-fold increase. It has been argued that rather than a real increment in frequency, diagnostic accuracy has improved, thus leading to detection of more cases. If that were the case, we would expect more chronic cases that started their disease in earlier times. This was not found in our patients; up to 1993 only 12% of all cases studied had more than 15 years of disease; this figure includes deceased patients. By contrast, the clinical onset of multiple sclerosis in most of our patients (88%) was within the past 15 years of the study, in 66% during the past 10 years (figure). If prevalence of multiple sclerosis in Mexico were stable, we would expect the inverse situation, more chronic cases with a long history of the disease.[10] The low frequency of familial multiple sclerosis in our patients (3%) stands in contrast with 10–15% in other western studies,[18] but it is similar to the 2% reported in Japan[11] where there is also the suspicion of a recent increase in cases of multiple sclerosis. Sadovnick *et al* reported a 5% susceptibility to multiple sclerosis in siblings and 4·5% in first cousins and second degree relatives.[20] By contrast, we found only 1·5 and 1·8% respectively. Moreover, all affected relatives were siblings and cousins, in no case were parents affected. This feature also supports the idea of a recent rise of genetic or environmental factors related to multiple sclerosis.

Foremost against the idea of a real increment in multiple sclerosis frequency is the absence of recent epidemiological studies that would give the final answer.[6] This report illustrates the urgent need to carry out epidemiological studies of multiple sclerosis in countries like Mexico immersed in the so called epidemiological transition, in which there is an apparent increase. Whether or not the real prevalence of multiple sclerosis is increasing, it is becoming one of the most important chronic neurological disorders in this country.

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